Denali Therapeutics Announces FDA Review Extension of BLA for Tividenofusp Alfa for the Treatment of MPS II (Hunter Syndrome)

October 13, 2025

SOUTH SAN FRANCISCO, Calif., Oct. 13, 2025 (GLOBE NEWSWIRE) -- Denali Therapeutics Inc. (Nasdaq: DNLI) today announced that the U.S. Food and Drug Administration (FDA) has extended its review timeline of the Biologics License Application (BLA) seeking accelerated approval of tividenofusp alfa for the treatment of mucopolysaccharidosis type II (MPS II), also known as Hunter syndrome. The Prescription Drug User Fee Act (PDUFA) target date has been extended from January 5, 2026, to April 5, 2026.

The extension follows Denali's submission of updated clinical pharmacology information in response to an information request from the FDA as part of the standard review process and is not related to efficacy, safety or biomarkers. The FDA classified the submission as a Major Amendment (MA) to the BLA, which, per FDA regulations, extends the review by three months. No additional data were requested by the FDA in the MA letter. Denali believes that the updated information submitted in the amendment does not affect the clinical pharmacology or benefit-risk conclusions of the BLA.

"We appreciate the FDA's continued collaboration throughout the review process," said Ryan Watts, Ph.D., Chief Executive Officer of Denali Therapeutics. "We continue to prepare for the potential approval and commercial launch of tividenofusp alfa. We feel the urgency to deliver for the MPS community, and we are committed to working together with regulators, physicians, and advocates to bring this important therapy to individuals and families living with Hunter syndrome."

About Tividenofusp Alfa

Tividenofusp alfa (DNL310) is composed of the iduronate 2-sulfatase (IDS) enzyme fused to Denali's proprietary TransportVehicle™ (TV) platform, designed to deliver IDS into the brain and the body, with the goal of addressing behavioral, cognitive and physical symptoms of Hunter syndrome (MPS II). The U.S. Food and Drug Administration has granted Fast Track and Breakthrough Therapy designations to tividenofusp alfa for development in the treatment of MPS II. The European Medicines Agency has granted Priority Medicines designation to tividenofusp alfa.

The Phase 2/3 COMPASS study is enrolling participants with MPS II in North America, South America and Europe to support global approval. Participants are randomized 2:1 to receive either tividenofusp alfa or idursulfase, respectively. More information about the COMPASS study can be found here.

Tividenofusp alfa is an investigational therapeutic and has not been approved for use by any Health Authority.

About Hunter Syndrome (MPS II)

Hunter syndrome, also known as MPS II, is a rare genetic lysosomal storage disease caused by mutations in the iduronate-2-sulfatase (IDS) gene. This results in a deficiency of the IDS enzyme, which is responsible for breaking down glycosaminoglycans (GAGs) such as heparan sulfate and dermatan sulfate. The accumulation of GAGs leads to progressive damage in multiple organs and tissues, including the brain. Symptoms of Hunter syndrome include developmental delays, cognitive decline, behavioral abnormalities and physical complications such as joint stiffness, hearing loss and organ dysfunction. Current standard-of-care enzyme replacement therapies do not cross the blood-brain barrier and therefore do not address the neurological symptoms of the disease. There is a significant unmet need for therapies that address both the central nervous system (CNS) and peripheral manifestations of Hunter syndrome.

About Denali Therapeutics

Denali Therapeutics is a biotechnology company developing a broad portfolio of product candidates engineered to cross the blood-brain barrier (BBB) for the treatment of neurodegenerative diseases and lysosomal storage diseases. Denali pursues new treatments by rigorously assessing genetically validated targets, engineering delivery across the BBB, and guiding development through biomarkers that demonstrate target and pathway engagement. Denali is based in South San Francisco. For additional information, please visit www.denalitherapeutics.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements expressed or implied in this press release include, plans, timelines and expectations relating to tividenofusp alfa, including the timing of the PDUFA action date, the likelihood of regulatory approval, expectations regarding the adequacy of clinical data to support the BLA, and the timing and likelihood of commercial launch; expectations for ongoing communications with the FDA; and statements made by Denali's Chief Executive Officer. Actual results may differ materially from those expressed or implied by these forward-looking statements due to a variety of risks and uncertainties. These include, but are not limited to, risks that the PDUFA action date may be extended and the FDA may ultimately determine not to approve the BLA in its present form or at all; risks arising from adverse economic conditions and their impact on Denali's business and operations;

the possibility of events or changes that could lead to the termination of Denali's collaboration agreements; challenges associated with Denali's transition to a late-stage clinical drug development company; the ability of Denali and its collaborators to complete the development and, if approved, the commercialization of product candidates; difficulties in patient enrollment for ongoing and future clinical trials; reliance on third-party manufacturers and suppliers for clinical trial materials; dependence on the successful development of Denali's blood-brain barrier platform technology and related programs; potential delays or failures in meeting expected clinical trial timelines; the risk that promising preclinical profiles may not be replicated in clinical settings; discrepancies between preclinical, early-stage, or preliminary clinical results and outcomes from later-stage trials; the occurrence of significant adverse events or other undesirable side effects; and the uncertainty surrounding regulatory approvals required for commercialization; Denali's ability to advance a pipeline of product candidates or develop commercially successful products; developments relating to Denali's competitors and its industry, including competing product candidates and therapies; Denali's ability to obtain, maintain, or protect intellectual property rights related to its product candidates; implementation of Denali's strategic plans for its business, product candidates, and blood-brain barrier platform technology; Denali's ability to obtain additional capital to finance its operations, as needed; Denali's ability to accurately forecast future financial results in the current environment; and other risks and uncertainties, including those described in Denali's most recent Annual and Quarterly Reports on Forms 10-K and 10-Q filed with the Securities and Exchange Commission (SEC) on February 27, 2025 and August 11, 2025, respectively, and Denali's future reports to be filed with the SEC. Denali's product candidates are investigational, and their safety and efficacy profiles have not yet been established. No Denali product candidates have been approved by any Health Authority for any use. Denali does not undertake any obligation to update or revise any forward-looking statements, to conform these statements to actual results or to make changes in Denali's expectations, except as required by law.

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